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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Fleischer and Reimer

Confirmation No.: 9935

Serial No.: 09/701,450

Group Art Unit: 1615

Filed: November 27, 2000

Examiner: Gollamudi S. Kishore

For: PREPARATIONS FOR THE APPLICATION OF ANTI-
INFLAMMATORY, ESPECIALLY ANTISEPTIC
AGENTS AND/OR AGENTS PROMOTING THE
HEALING OF WOUNDS TO THE LOWER
RESPIRATORY TRACT

Attorney Docket No.: 11390-005-999

PRE-APPEAL BRIEF CONFERENCE REQUEST

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicants hereby request review of the Final Rejection mailed March 28, 2006 ("Final Rejection") of the above-captioned application prior to filing an appeal brief for the reasons set forth below. Applicants submit that the Final Rejection fails to establish a *prima facie* rejection and that the evidence and arguments previously submitted by Applicants is nonetheless sufficient to overcome the Final Rejection. A Notice of Appeal is submitted herewith accompanied by the appropriate fee.

The present invention is directed to methods for treating an infection in the lower respiratory tract by administering to a patient, in need thereof, liposomes containing povidone iodine in an amount sufficient to treat the infection. Additional claims specify the size of the liposomes, as well as specify that the liposomes can contain additional agents, such as anesthetic agents, wound healing agents, corticosteroids and antibiotics.

Independent claim 22 and dependent claims 32, 33, 36-41, 51, 55-61, 64-68 and 71-74 remain rejected under 35 U.S.C. § 103(a) as allegedly obvious over European Patent No. 639373 ("the '373 patent") in combination with either U.S. Patent No. 5,049,388 to Knight *et al.* ("Knight"), or U.S. Patent No. 5,049,389 to Radhakrishnan ("Radhakrishnan"), or U.S. Patent

No. 5,290,540 to Prince ("Prince") or *vice versa*. Additionally, in a second Section 103 rejection, independent claim 22 and dependent claims 32, 33, 36-41, 51, 55-61, 64-68 and 71-74 remain rejected under 35 U.S.C. § 103(a) as allegedly obvious over the '373 patent in combination with Knight or Radhakrishnan or Prince or *vice versa*, further in combination with International Patent Publication No. WO 85/00112 ("the '112 Publication"). Applicants disagree and respectfully submit that such methods are not taught, much less suggested, by the references cited by the Examiner. Applicants submit that the rejection is improperly made as there is no suggestion for combining the references, especially in view of the fact that skin or eye tissue is not equivalent to the tissue found in the lower respiratory tract. Moreover, Applicants respectfully submit that the Examiner is engaging in impermissible hindsight analysis.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, the prior art reference(s) must teach or suggest all the claim limitations. Second, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Third, there must be a reasonable expectation of success. A *prima facie* case of obviousness has not been made with regard to the pending claims.

The '373 patent teaches that liposomes containing povidone iodine can be used externally to treat infections, including in the eye. The '373 patent provides absolutely no teaching for methods of treating an infection internally in the body, much less in the lower respiratory tract. Moreover, with regard to the Examiner's comment that the '373 Patent teaches the use of povidone iodine to treat an infection at a mucous membrane, the Examiner fails to realize that when the '373 Patent disclosure is read in its entirety, only external mucous membranes such as the eye are within the scope of the disclosure of the '373 Patent.

The disclosures of Knight, Radhakrishnan and Prince, which are each interchangeable in the current analysis, do not fill in the gap between the '373 Patent and the claimed invention. All three references relate to the use of liposomal formulations, *inter alia*, for the treatment of lung diseases. None of these references teaches or suggests liposomes containing povidone iodine, much less that such povidone iodine-containing liposomes can be used in the methods of the invention for treating an infection in the lower respiratory tract. They merely teach that liposomes can be administered to the lung. These references do not teach or suggest that povidone iodine can be administered to the lung or lower respiratory tract. Since there is no

teaching or suggestion in the art for using liposomes containing iodine treat infections internally, the Examiner has not met the requirements for a *prima facie* rejection for obviousness.

Moreover, Applicants note that none of the substances taught by Knight, Radhakrishnan or Price to be administered to the lung in liposomes are similar to povidone iodine, which is an aggressive oxidizing antiseptic. Since none of the types of compounds disclosed by Knight, Radhakrishnan or Price are equivalent to the type of compound that is povidone iodine, no comparison can be made between the suitability to administer any of the compounds taught by Knight, Radhakrishnan or Price to administering povidone iodine. The Examiner merely alleges, without any substantiation, that the teaching in the '373 patent for applications to external mucous membranes and the eye is "suggestive of the safe application of the compositions even for nasal oral or tracheal mucous tissues." However, this is mere unsupported speculation on the Examiner's part.

Further, attention is directed to the Declaration of Dr. Wolfgang Fleischer under 37 C.F.R. § 1.132 ("Rule 132 Declaration"), in which Dr. Fleischer, a co-inventor of the claimed subject matter, states that it is his belief that the compounds disclosed by the cited references are not comparable to povidone iodine and are not suggestive that povidone iodine could be administered safely to the lower respiratory tract (Rule 132 Declaration, § 5).

Applicants note that the Examiner is wrongly assuming that a compound applicable to the skin and eye is automatically applicable to the alveoli, bronchi and trachea of the lower respiratory tract. It is well known that lung tissue has a different function from, and is very different in structure from skin or eye or from any other mucous membrane, and that these tissues have different sensitivities to different agents. For example, the cells of the lower respiratory tract contain ciliated cells and specialized mucous secreting cells, and it is in the lower respiratory tract that gas exchange occurs. This lung tissue is highly sensitive and damaging such tissue can lead to severe illness, if not death. As evidence of the foregoing, Applicants directed the Examiner's attention to Powell *et al.*, 2003, Chapter 18, Structure and Function of the Respiratory System, in Essential Medical Physiology, 3rd Edition, Leonard R. Johnson, Ed., Elsevier Academic Press, New York, pp. 259-276 ("Powell") which was attached as Exhibit A to the Declaration. Powell teaches the structure of the respiratory tract and the specialized cells in each part of the respiratory tract, as well as the respiratory and non-respiratory functions of the lung and sub-parts thereof. It is clear that these lung tissues are very different from skin, eye and the mucous membranes of the upper respiratory tract, including the nasal passages.

With regard to the Examiner's second Section 103 rejection citing the same references above in combination with the '112 Publication, Applicants submit that this reference also fails to fill in the gap between the claimed invention and the previously cited prior art. The '112 Publication teaches that microbiocidal agents, including povidone iodine, can be administered by inhalation of a stream or heated air containing the agents to the nasal passages only, which are in the upper respiratory tract. It is clear that the administration is only to the nasal passages, not to any other part of the respiratory tract, much less the lower respiratory tract. There is no teaching or suggestion that liposomes containing povidone iodine can be administered to the lower respiratory tract to treat an infection. As the nasal passages are a different tissue as compared to the tissue of the lower respiratory tract, application to the nasal passage is not suggestive of the lower respiratory tract. See the Rule 132 Declaration, § 6.

Applicants remain in their belief that the Examiner is subconsciously using hindsight reconstruction and has simply combined prior art references without evidence of the required suggestion, teaching or motivation. The Federal Circuit has stated that the best defense against a hindsight-based obviousness analysis is rigorous application for the requirement for a showing of the teaching or motivation to combine the prior art references. *In re Dembiczak*, 175 F.3d 994, 50 U.S.P.Q.2d 1614 (Fed. Cir. 1999). In the instant application, Applicants submit that the Examiner has not provided the required suggestion, teaching or motivation to combine the teachings of the '373 patent with the teachings of Knight or Radhakrishnan or Prince or the '112 Publication since none the compounds taught in the cited art is suggestive of povidone iodine and/or since the tissues where povidone iodine has previously been applied are not suggestive of the tissues of the lower respiratory tract. Thus, Applicants respectfully submit that these Section 103 rejections are in error and request that these rejections be withdrawn.

CONCLUSION

For at least the reasons above, Applicants submit that independent claim 22 is in condition for allowance. As claims 32, 33, 36-41, 51, 55-61, 64-68 and 71-74 depend from independent claim 22, Applicants submit that these claims are likewise in condition for allowance.

Applicants request that the undersigned be contacted at (212) 326-3921 if any questions or issues remain.

Respectfully submitted,

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